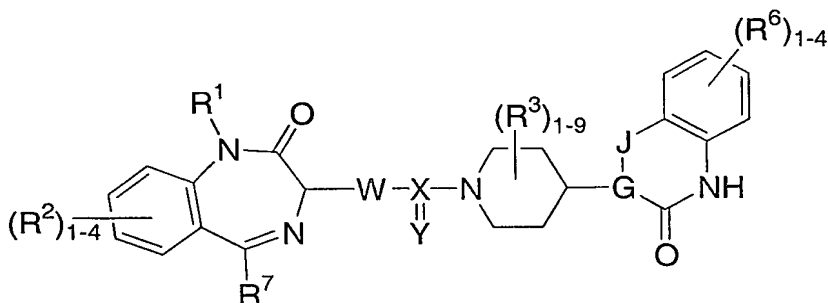


WHAT IS CLAIMED IS:

1. A compounds of formula I:



I

wherein:

R^1 is selected from:

- 1) H, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, and heterocycle, unsubstituted or substituted with one or more substituents independently selected from:
 - a) C_1 - C_6 alkyl,
 - b) C_3 - C_6 cycloalkyl,
 - c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - f) $(F)_p C_{1-3}$ alkyl,
 - g) halogen,
 - h) OR^4 ,
 - i) $O(CH_2)_s OR^4$,
 - j) CO_2R^4 ,
 - k) $(CO)NR^{10}R^{11}$,
 - l) $O(CO)NR^{10}R^{11}$.

- 5
- m) $N(R^4)(CO)NR^{10}R^{11}$,
 - n) $N(R^{10})(CO)R^{11}$,
 - o) $N(R^{10})(CO)OR^{11}$,
 - p) $SO_2NR^{10}R^{11}$,
 - q) $N(R^{10})SO_2R^{11}$,
 - r) $S(O)_mR^{10}$,
 - s) CN ,
 - t) $NR^{10}R^{11}$,
 - u) $N(R^{10})(CO)NR^4R^{11}$, and
 - 10 v) $O(CO)R^4$; and
- 2) aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from:
- 15
- a) C_{1-6} alkyl,
 - b) C_{3-6} cycloalkyl,
 - c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - 20 e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
 - f) $(F)_pC_{1-3}$ alkyl,
 - g) halogen,
 - h) OR^4 ,
 - 25 i) $O(CH_2)_sOR^4$,
 - j) CO_2R^4 ,
 - k) $(CO)NR^{10}R^{11}$,
 - l) $O(CO)NR^{10}R^{11}$,
 - m) $N(R^4)(CO)NR^{10}R^{11}$,
 - 30 n) $N(R^{10})(CO)R^{11}$,
 - o) $N(R^{10})(CO)OR^{11}$,
 - p) $SO_2NR^{10}R^{11}$,
 - q) $N(R^{10})SO_2R^{11}$,
 - r) $S(O)_mR^{10}$,

- s) CN,
- t) $\text{NR}^{10}\text{R}^{11}$,
- u) $\text{N}(\text{R}^{10})(\text{CO})\text{NR}^4\text{R}^{11}$; and
- v) $\text{O}(\text{CO})\text{R}^4$; and

5

R^2 is independently selected from H and:

- 1) C_{1-6} alkyl,
- 2) C_{3-6} cycloalkyl,
- 10 3) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
- 4) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,
- 5) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are
- 15 independently selected from R^4 ,
- 6) $(\text{F})_p\text{C}_{1-3}$ alkyl,
- 7) halogen,
- 8) OR^4 ,
- 9) $\text{O}(\text{CH}_2)_s\text{OR}^4$,
- 20 10) CO_2R^4 ,
- 11) $(\text{CO})\text{NR}^{10}\text{R}^{11}$,
- 12) $\text{O}(\text{CO})\text{NR}^{10}\text{R}^{11}$,
- 13) $\text{N}(\text{R}^4)(\text{CO})\text{NR}^{10}\text{R}^{11}$,
- 14) $\text{N}(\text{R}^{10})(\text{CO})\text{R}^{11}$,
- 25 15) $\text{N}(\text{R}^{10})(\text{CO})\text{OR}^{11}$,
- 16) $\text{SO}_2\text{NR}^{10}\text{R}^{11}$,
- 17) $\text{N}(\text{R}^{10})\text{SO}_2\text{R}^{11}$,
- 18) $\text{S}(\text{O})_m\text{R}^{10}$,
- 19) CN,
- 30 20) $\text{NR}^{10}\text{R}^{11}$,
- 21) $\text{N}(\text{R}^{10})(\text{CO})\text{NR}^4\text{R}^{11}$, and
- 22) $\text{O}(\text{CO})\text{R}^4$;

R^7 is selected from:

1) H, C₀-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-₆ cycloalkyl and heterocycle, unsubstituted or substituted with one or more substituents independently selected from:

- a) C₁₋₆ alkyl,
- b) C₃₋₆ cycloalkyl,
- c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R⁴,
- d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R⁴,
- e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R⁴,
- f) (F)_pC₁₋₃ alkyl,
- g) halogen,
- h) OR⁴,
- i) O(CH₂)_sOR⁴,
- j) CO₂R⁴,
- k) (CO)NR¹⁰R¹¹,
- l) O(CO)NR¹⁰R¹¹,
- m) N(R⁴)(CO)NR¹⁰R¹¹,
- n) N(R¹⁰)(CO)R¹¹,
- o) N(R¹⁰)(CO)OR¹¹,
- p) SO₂NR¹⁰R¹¹,
- q) N(R¹⁰) SO₂R¹¹,
- r) S(O)_mR¹⁰,
- s) CN,
- t) NR¹⁰R¹¹,
- u) N(R¹⁰)(CO)NR⁴R¹¹,
- v) O(CO)R⁴; and

2) aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from:

- a) C₁₋₆ alkyl,
- b) C₃₋₆ cycloalkyl,

c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,

d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,

e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R^4 ,

f) $(F)_p C_{1-3}$ alkyl,

g) halogen,

h) OR^4 ,

i) $O(CH_2)_s OR^4$,

j) $CO_2 R^4$,

k) $(CO)NR^{10}R^{11}$,

l) $O(CO)NR^{10}R^{11}$,

m) $N(R^4)(CO)NR^{10}R^{11}$,

n) $N(R^{10})(CO)R^{11}$,

o) $N(R^{10})(CO)OR^{11}$,

p) $SO_2 NR^{10}R^{11}$,

q) $N(R^{10}) SO_2 R^{11}$,

r) $S(O)_m R^{10}$,

s) CN,

t) $NR^{10}R^{11}$,

u) $N(R^{10})(CO)NR^4 R^{11}$, and

v) $O(CO)R^4$;

R^4 is selected from: H, C_{1-6} alkyl, $(F)_p C_{1-6}$ alkyl, C_{3-6} cycloalkyl, aryl, heteroaryl and benzyl, unsubstituted or substituted with halogen, hydroxy or C_{1-6} alkoxy;

R^5 is independently selected from H, substituted or unsubstituted C_{1-6} alkyl, C_{3-6} cycloalkyl, aryl, heteroaryl, OR^4 , $N(R^4)_2$, $CO_2 R^4$ and $(F)_p C_{1-6}$ alkyl;

W is O, NR^4 or $C(R^4)_2$;

X is C or S;

Y is O, (R⁴)₂, NCN, NSO₂CH₃ or NCONH₂, or Y is O₂ when X is S;

R³ is independently selected from H, substituted or unsubstituted C₁-C₃ alkyl, CN and CO₂R⁴;

5 R⁶ is independently selected from H and:

- a) C₁-6 alkyl,
- b) C₃-6 cycloalkyl,
- c) aryl, unsubstituted or substituted with 1-5 substituents where
10 the substituents are independently selected from R⁴,
- d) heteroaryl, unsubstituted or substituted with 1-5 substituents
where the substituents are independently selected from R⁴,
- e) heterocycle, unsubstituted or substituted with 1-5 substituents
where the substituents are independently selected from R⁴,
- 15 f) (F)_pC₁₋₃ alkyl,
- g) halogen,
- h) OR⁴,
- i) O(CH₂)_sOR⁴,
- j) CO₂R⁴,
- 20 k) (CO)NR¹⁰R¹¹,
- l) O(CO)NR¹⁰R¹¹,
- m) N(R⁴)(CO)NR¹⁰R¹¹,
- n) N(R¹⁰)(CO)R¹¹,
- o) N(R¹⁰)(CO)OR¹¹,
- 25 p) SO₂NR¹⁰R¹¹,
- q) N(R¹⁰)SO₂R¹¹,
- r) S(O)_mR¹⁰,
- s) CN,
- t) NR¹⁰R¹¹,
- 30 u) N(R¹⁰)(CO)NR⁴R¹¹, and
- v) O(CO)R⁴;

R¹⁰ and R¹¹ are independently selected from: H, C₁-6 alkyl, (F)_pC₁₋₆ alkyl, C₃-6 cycloalkyl, aryl, heteroaryl and benzyl, unsubstituted or substituted with halogen, hydroxy or C₁-C₆ alkoxy, where R¹⁰

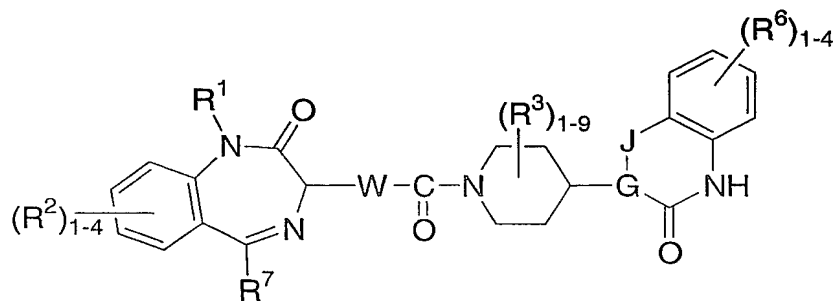
and R¹¹ may be joined together to form a ring selected from: azetidiny, pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl, which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R⁴;

5 G-J is selected from: N, N-C(R⁵)₂, C=C(R⁵), C=N; C(R⁵), C(R⁵)-C(R⁵)₂, C(R⁵)-C(R⁵)₂-C(R⁵)₂, C=C(R⁵)-C(R⁵)₂, C(R⁵)-C(R⁵)=C(R⁵), C(R⁵)-C(R⁵)₂-N(R⁵), C=C(R⁵)-N(R⁵), C(R⁵)-C(R⁵)=N, C(R⁵)-N(R⁵)-C(R⁵)₂, C=N-C(R⁵)₂, C(R⁵)-N=C(R⁵), C(R⁵)-N(R⁵)-N(R⁵), C=N-N(R⁵), N-C(R⁵)₂-C(R⁵)₂, N-C(R⁵)=C(R⁵), N-C(R⁵)₂-N(R⁵), N-C(R⁵)=N, N-N(R⁵)-C(R⁵)₂ and N-N=C(R⁵);

10 p is 0 to 2q+1, for a substituent with q carbons;
 m is 0, 1 or 2;
 n is 0 or 1;
 s is 1, 2 or 3;

15 and pharmaceutically acceptable salts and individual diastereomers thereof.

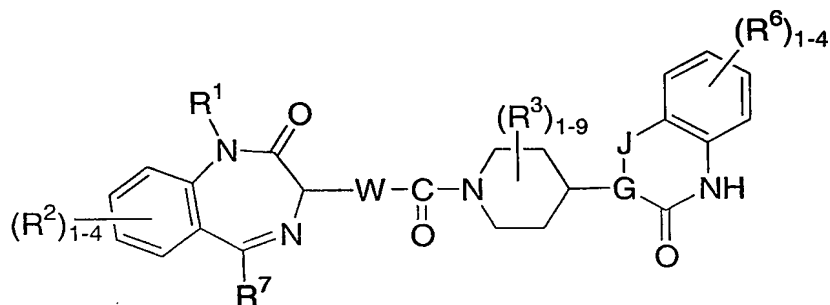
2. The compound of claim 1 of the formula Ia:



20 and pharmaceutically acceptable salts and individual diastereomers thereof.

3. The compound of claim 1 of the formula Ia:

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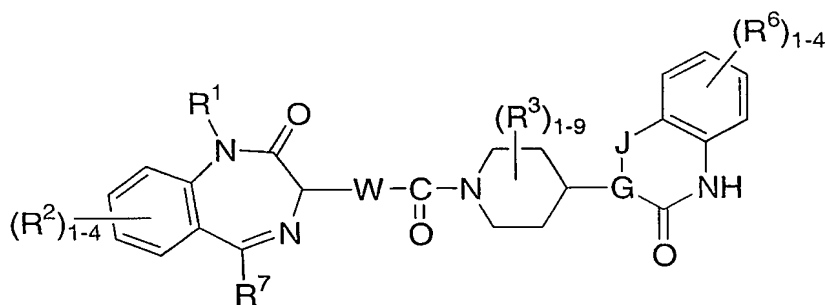


wherein R^7 is phenyl, unsubstituted or substituted with one or substituents independently selected from:

- a) C_{1-6} alkyl,
- b) OH,
- c) OR^5 ,
- d) halogen,
- e) CO_2R^4 ,
- f) $S(O)_mR^5$,
- g) $N(R^4)_2$, and
- j) CN,

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of claim 1 of the formula Ia:

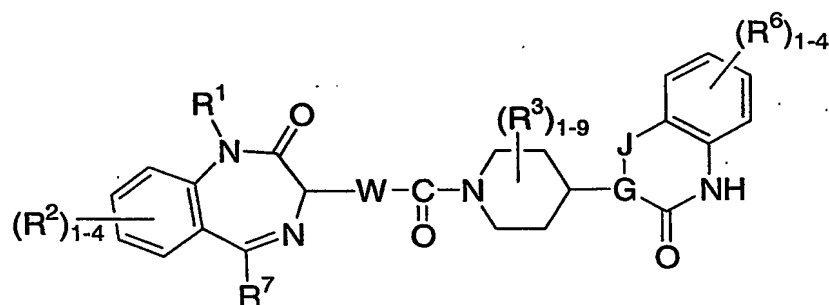


wherein R^7 is heteroaryl, unsubstituted or substituted with one or substituents independently selected from:

- a) C₁₋₆ alkyl,
- b) OH,
- c) OR⁵,
- d) halogen,
- e) CO₂R⁴,
- f) S(O)_mR⁵,
- g) N(R⁴)₂, and
- j) CN,

and pharmaceutically acceptable salts and individual diastereomers thereof.

5. The compound of claim 1 of the formula Ia:

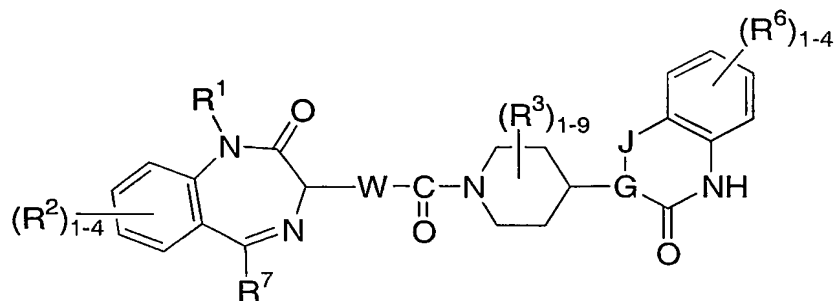


wherein R⁷ is selected from H and C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₃₋₆ cycloalkyl, unsubstituted or substituted with one or substituents independently selected from:

- a) C₁₋₆ alkyl,
- b) C₁₋₆ alkoxy,
- c) fluorine,
- d) HO,
- e) OR⁵,
- f) CO₂R⁴,
- g) CON(R⁴)₂,
- h) S(O)_mR⁵, and
- i) N(R⁴)₂; and

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of claim 1 of the formula Ia:

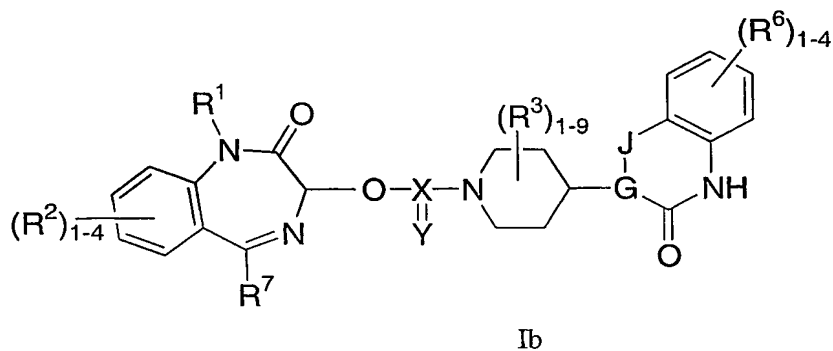


wherein R^7 is heterocycle, unsubstituted or substituted with one or substituents independently selected from:

- a) C_{1-6} alkyl,
- b) C_{1-6} alkoxy,
- c) fluorine,
- d) HO,
- e) OR^5 ,
- f) CO_2R^4 ,
- g) $CON(R^4)_2$,
- h) $S(O)_mR^5$, and
- i) $N(R^4)_2$; and

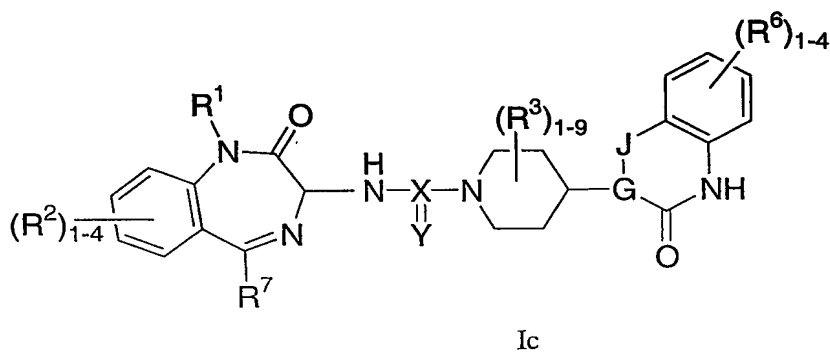
and pharmaceutically acceptable salts and individual diastereomers thereof.

7. The compound of claim 1 of the formula Ib:



5 and pharmaceutically acceptable salts and individual diastereomers thereof.

8. The compound of claim 1 of the formula Ic:

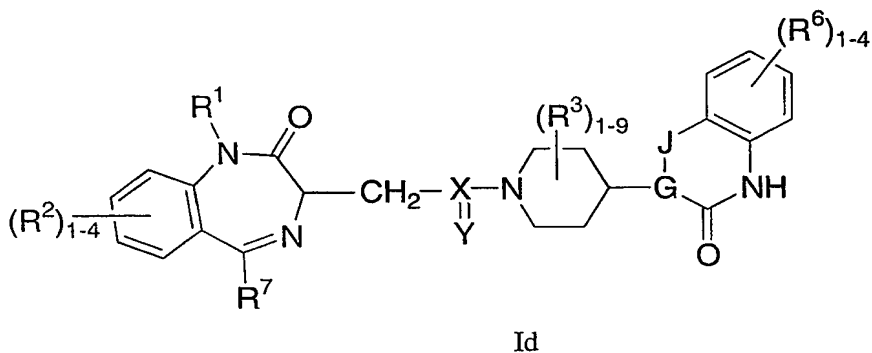


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and pharmaceutically acceptable salts and individual diastereomers thereof.

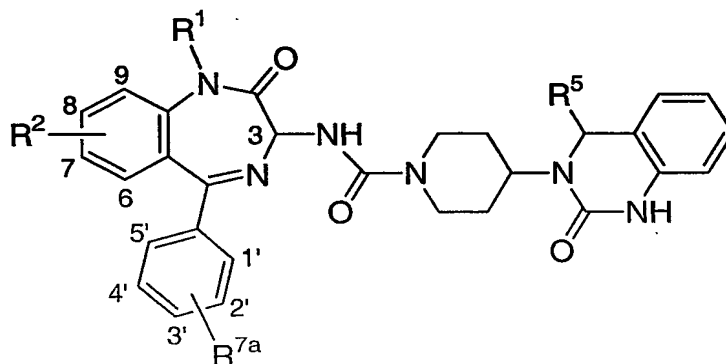
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9. The compound of claim 1 of the formula Id:



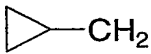
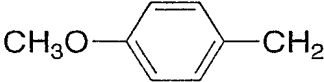
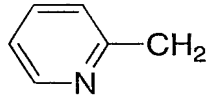
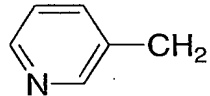
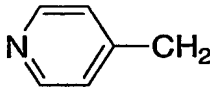
5 and pharmaceutically acceptable salts and individual diastereomers thereof.

10. The compound of claim 1 of the formula:



10 wherein R¹, R², R^{7a} and R⁵, and the configuration of C-3, are selected from a single row in the the following table:

C-3	R ¹	R ²	R ^{7a}	R ⁵
R	CH ₃	H	H	H
S	CH ₃	H	H	H

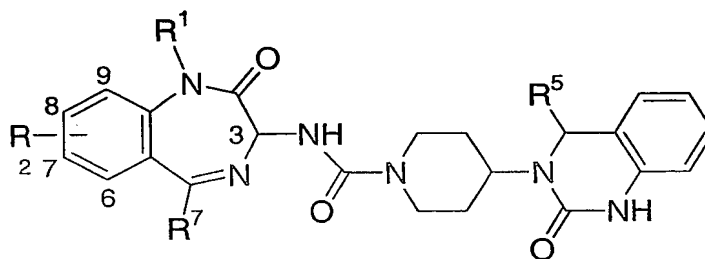
R	CF ₃ CH ₂	H	H	H
R	CF ₃ CH ₂	6-Cl	H	H
R	CF ₃ CH ₂	7-Cl	H	H
R	CF ₃ CH ₂	8-Cl	H	H
R	CF ₃ CH ₂	9-Cl	H	H
R,S	<i>n</i> -C ₃ H ₇	H	H	H
R,S	<i>i</i> -C ₃ H ₇	H	H	H
R,S	<i>n</i> -C ₄ H ₇	H	H	H
R	<i>i</i> -C ₄ H ₇	H	H	H
S	<i>i</i> -C ₄ H ₇	H	H	H
R,S	<i>n</i> -CF ₃ (CH ₂) ₃	H	H	H
R,S	 CH ₂	H	H	H
R,S	 CH ₂	H	H	H
R,S	 CH ₂	H	H	H
R,S	 CH ₂	H	H	H
R,S	 CH ₂	H	H	H

R,S	<i>i</i> -C ₃ H ₇	H	2'-F	H
R,S	<i>i</i> -C ₃ H ₇	H	2'-F	OH
R,S	<i>i</i> -C ₄ H ₉	H	2'-F	H
R,S	<i>i</i> -C ₄ H ₉	H	2'-F	OH
R,S	CF ₃ CH ₂	H	2'-F	H
R,S	CF ₃ CH ₂	H	4'-F	H
R,S	CF ₃ CH ₂	H	4'-F	OH

and pharmaceutically acceptable salts and individual diastereomers thereof.

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11. The compound of claim 1 of the formula:



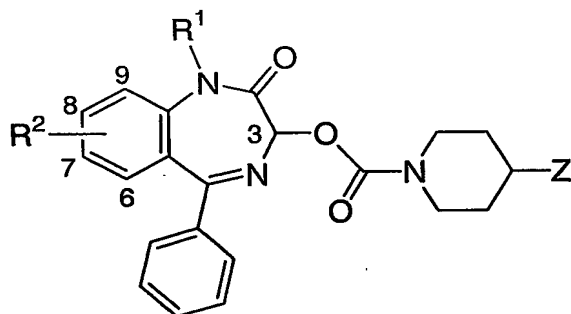
10 wherein R¹, R², R⁷ and R⁵, and the configuration of C-3, are selected from a single row in the following table:

C-3	R ¹	R ²	R ⁷	R ⁵
R	CH ₃	H	Cyclohexyl	H
R	CF ₃ CH ₂	H	<i>i</i> -C ₃ H ₇	H

R,S	CH ₃	7- CH ₃	<i>i</i> -C ₃ H ₇	H
R,S	CH ₃	8- CH ₃	<i>i</i> -C ₃ H ₇	H
S	CF ₃ CH ₂	H	<i>t</i> -C ₄ H ₉	H

and pharmaceutically acceptable salts and individual diastereomers thereof.

12. The compound of claim 1 of the formula:



wherein R¹, R² and Z, and the configuration of C-3, are selected from a single row in the following table:

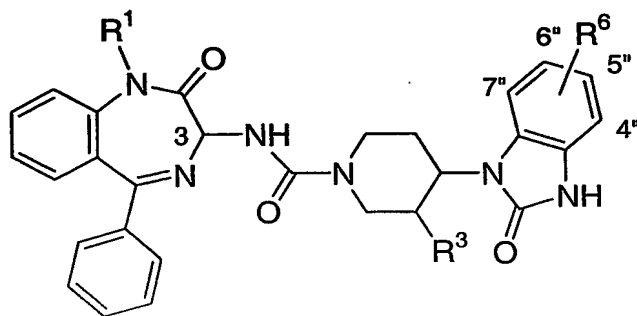
C-3	R ¹	R ²	Z
R,S	CH ₃	H	
R,S	CH ₃	7-Cl	

R,S	CF ₃ CH ₂	H	
R,S	CF ₃ CH ₂	H	

and pharmaceutically acceptable salts and individual diastereomers thereof.

13. The compound of claim 1 of the formula:

5



wherein R¹, R³ and R⁶, and the configuration of C-3, are selected from a single row in the following table:

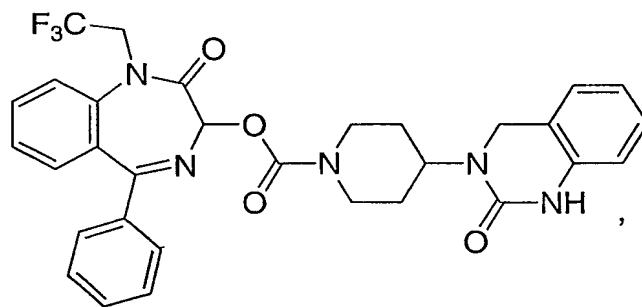
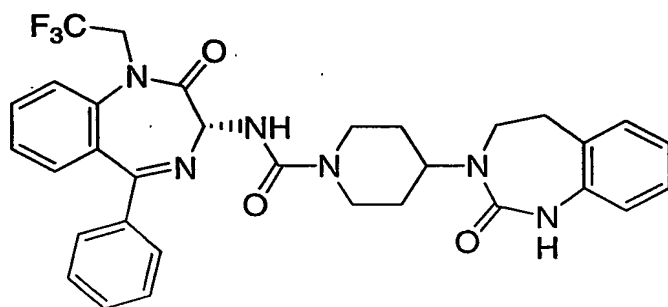
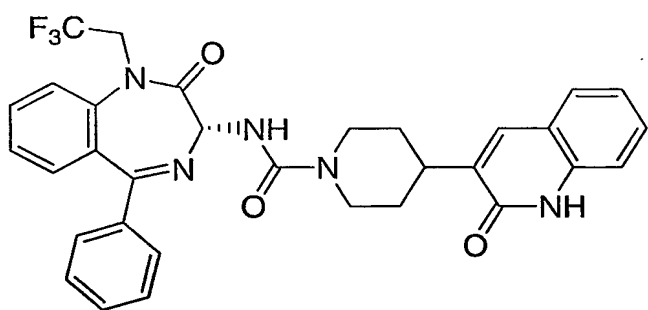
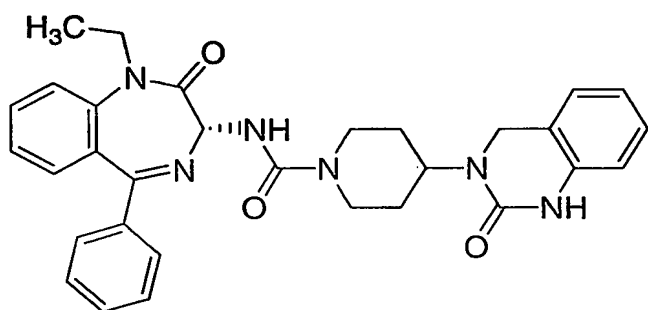
C-3	R ¹	R ³	R ⁶
R	CF ₃ CH ₂	H	H
R	CF ₃ CH ₂	H	5''-CH ₃
R	CF ₃ CH ₂	H	6''-F

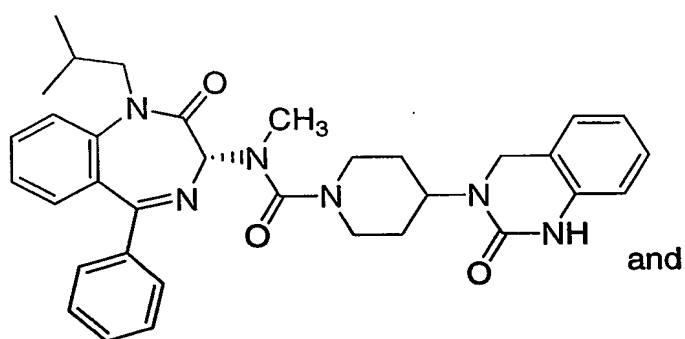
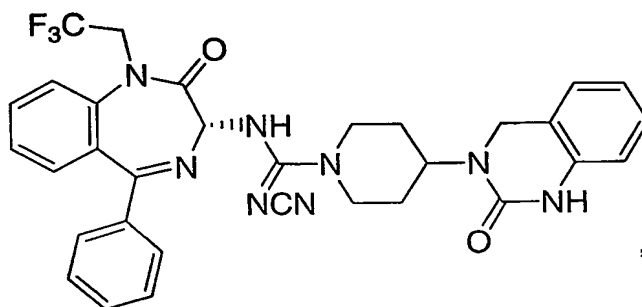
R	CF ₃ CH ₂	CH ₃	H
R	CF ₃ CH ₂	H	7''-Cl
R	CF ₃ CH ₂	H	6''-CH ₃
R	CF ₃ CH ₂	H	6''-CF ₃
R	CF ₃ CH ₂	H	6''-F
R	CF ₃ CH ₂	H	6''-CO ₂ H
R	CF ₃ CH ₂	H	6''-CONH ₂
R	CF ₃ CH ₂	H	6''-SO ₂ CH ₃
R	CF ₃ CH ₂	H	5''-CH ₃
R	CF ₃ CH ₂	H	5''-Cl
R	CF ₃ CH ₂	H	4''-CH ₃
R	CF ₃ CH ₂	H	5''-F

and pharmaceutically acceptable salts and individual diastereomers thereof.

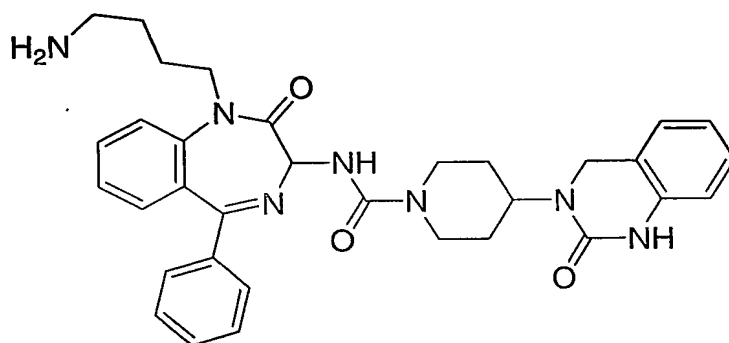
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14. A compound selected from:





and



10 and pharmaceutically acceptable salts and individual diastereomers thereof.

15. A pharmaceutical composition which comprises an inert carrier and the compound of Claim 1.

16. A method for antagonism of CGRP receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 1.

5 17. A method for treating, controlling, ameliorating or reducing the risk of headache, migraine or cluster headache in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of the compound of Claim 1.

10 18. A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:
a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

15 a therapeutically effective amount of a second agent selected from serotonin agonists, analgesics, anti-inflammatory agents, anti-hypertensives and anticonvulsants.

19. The method of claim 18, wherein said second agent is selected from a $5HT_{1B/1D}$ agonist, a $5HT_{1D}$ agonist, and a $5HT_{1F}$ agonist.

20 20. The method of claim 19, wherein said second agent is selected from rizatriptan, sumatriptan, naratriptan, zolmitriptan, almotriptan, eletriptan, avitriptan, frovatriptan, LY334370 and PNU-142633.

25 21. The method of claim 18, wherein said second agent is selected from ergotamine and dihydroergotamine.

22. The method of claim 18, wherein said second agent is aspirin or acetaminophen.

30 23. The method of claim 18, wherein said second agent is a glucocorticoid.

24. The method of claim 18, wherein said second agent is a non-steroidal anti-inflammatory agent.

25. The method of claim 24, wherein said second agent is selected from ibuprofen, ketoprofen, fenoprofen, naproxen, indomethacin, sulindac, meloxicam, piroxicam, tenoxicam, lornoxicam, ketorolac, etodolac, mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid, diclofenac, oxaprozin, apazone, nimesulide, nabumetone, tenidap, etanercept, tolmetin, phenylbutazone, oxyphenbutazone, diflunisal, salsalate, olsalazine and sulfasalazine.

26. The method of claim 18, wherein said second agent is an anticonvulsant selected from topiramate, zonisamide, divalproex sodium, pregabalin, gabapentin, levetiracetam, lamotrigine and tiagabine.

27. The method of claim 18, wherein said second agent is an anti-hypertensive selected from angiotensin II antagonists, angiotensin I antagonists, angiotensin converting enzyme inhibitors, and renin inhibitors.

28. The method of claim 27, wherein said second agent is selected from losartan, candesartan, candesartan cilexetil, irbesartan, valsartan, eprosartan, telmisartan, olmesartan, medoxomil, captopril, benazepril, quinapril, perindopril, ramipril, trandolapril, lisinopril, and enalapril

29. A method of treating or preventing migraine headaches, cluster headaches, and headaches, comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from anti-anxiety agents and neuroleptics.

30. The method of claim 29, wherein said second agent is selected from, diazepam, alprazolam, chlordiazepoxide, olanzapine, droperidol, prochlorperazine, chlorpromazine and quetiapine.

31. A method of treating or preventing migraine headaches, cluster headaches, and headaches, comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from beta-blockers and calcium channel blockers.

5 32. The method of claim 31, wherein said second agent is selected from timolol, propanolol, atenolol, metoprolol, nadolol, flunarizine, diltiazem, amlodipine, felodipine, nisolipine, isradipine, nimodipine, lomerizine, verapamil, nifedipine, prochlorperazine and civamide.

10 33. A method of treating or preventing migraine headaches, cluster headaches, and headaches, comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

15 a therapeutically effective amount of a second agent selected from anti-depressants, selective serotonin reuptake inhibitors, and NE reuptake inhibitors.

20 34. The method of claim 33, wherein said second agent is selected from amitriptyline, nortriptyline, clomipramine, imipramine, venlafaxine, doxepin, protriptyline, desipramine, trimipramine, fluoxetine, paroxetine, sertraline, duloxetine, escitalopram, and citalopram.

 35. A method of treating or preventing migraine headaches, cluster headaches, and headaches, comprising the co-administration, to a person in need of such treatment, of:

25 a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from botulinum toxins A or B.

30 36. A method of treating or preventing migraine headaches, cluster headaches, and headaches, comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from vanilloid receptor antagonists, adenosine 1 antagonists, NR2B antagonists, substance P antagonists, granzyme B inhibitors, endothelin antagonists, norepinephrin precursors, nitric oxide synthase inhibitors, neuroleptics, bradykinin
5 antagonists, gap junction inhibitors, AMPA/KA antagonists, sigma receptor agonists, chloride channel enhancers, monoamine oxidase inhibitors, opioid agonists, and leukotriene receptor antagonists.

37. The method of claim 36, wherein said second agent is selected from montelukast
and zafirlukast.

38. The method of claim 36, wherein said second agent is aprepitant.

39. A method of treating or preventing migraine headaches, cluster headaches, and
headaches, comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt
thereof; and

a therapeutically effective amount of a second agent selected from the group consisting of anti-emetics,
prokinetics, and histamine H1 antagonists.

40. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt
thereof; and

a therapeutically effective amount of a second agent selected from serotonin agonists, analgesics, anti-
inflammatory agents, and anticonvulsants.

41. The composition of claim 40, wherein said second agent is selected from a
5HT_{1B/1D} agonist, a 5HT_{1D} agonist, and a 5HT_{1F} agonist.

42. The composition of claim 41, wherein said second agent is selected from rizatriptan, sumatriptan, naratriptan, zolmitriptan, almotriptan, eletriptan, avitriptan, frovatriptan, LY334370 and PNU-142633.

5 43. The composition of claim 40, wherein said second agent is selected from ergotamine and dihydroergotamine.

44. The composition of claim 40, wherein said second agent is aspirin or acetaminophen.

10 45. The composition of claim 40, wherein said second agent is a glucocorticoid.

46. The composition of claim 40, wherein said second agent is a non-steroidal anti-inflammatory agent.

15 47. The composition of claim 46, wherein said second agent is selected from ibuprofen, ketoprofen, fenoprofen, naproxen, indomethacin, sulindac, meloxicam, piroxicam, tenoxicam, lornoxicam, ketorolac, etodolac, mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid, diclofenac, oxaprozin, apazone, nimesulide, nabumetone, tenidap, etanercept, tolmetin, phenylbutazone, oxyphenbutazone, diflunisal, salsalate, olsalazine and sulfasalazine.

20 48. The composition of claim 40, wherein said second agent is an anticonvulsant selected from topiramate, zonisamide, divalproex sodium, pregabalin, gabapentin, levetiracetam, lamotrigine and tiagabine.

25 49. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

30 a therapeutically effective amount of a second agent selected from angiotensin II antagonists, angiotensin I antagonists, angiotensin converting enzyme inhibitors, and renin inhibitors.

50. The composition of claim 49, wherein said second agent is selected from losartan, candesartan, candesartan cilexetil, irbesartan, valsartan, eprosartan, telmisartan, olmesartan, medoxomil, captopril, benazepril, quinapril, perindopril, ramipril, trandolapril, lisinopril, and enalapril.

5 51. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

10 a therapeutically effective amount of a second agent selected from anti-anxiety agents and neuroleptics.

52. The composition of claim 51, wherein said second agent is selected from, diazepam, alprazolam, chlordiazepoxide, olanzapine, droperidol, prochlorperazine, chlorpromazine and quetiapine.

15 53. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

20 a therapeutically effective amount of a second agent selected from beta-blockers and calcium channel blockers.

54. The composition of claim 53, wherein said second agent is selected from
25 timolol, propranolol, atenolol, metoprolol, nadolol, flunarizine, diltiazem, amlodipine, felodipine, nisolipine, isradipine, nimodipine, lomerizine, verapamil, nifedipine, prochlorperazine and civamide.

55. A pharmaceutical composition comprising:

30 a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from anti-depressants, selective serotonin reuptake inhibitors, and NE reuptake inhibitors.

56. The composition of claim 55, wherein said second agent is selected from amitriptyline, nortriptyline, clomipramine, imipramine, venlafaxine, doxepin, protriptyline, desipramine, trimipramine, fluoxetine, paroxetine, sertraline, duloxetine, escitalopram, and citalopram.

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57. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

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a therapeutically effective amount of a second agent selected from botulinum toxins A or B.

58. A pharmaceutical composition comprising:

15 a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from vanilloid receptor antagonists, adenosine 1 antagonists, NR2B antagonists, substance P antagonists, granzyme B inhibitors, endothelin antagonists, norepinephrin precursors, nitric oxide synthase inhibitors, neuroleptics, bradykinin antagonists, gap junction inhibitors, AMPA/KA antagonists, sigma receptor agonists, chloride channel enhancers, monoamine oxidase inhibitors, opioid agonists, and leukotriene receptor antagonists.

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59. The composition of claim 58, wherein said second agent is selected from montelukast and zafirlukast.

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60. The composition of claim 58, wherein said second agent is aprepitant.

61. A pharmaceutical composition comprising:

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a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from the group consisting of anti-emetics, prokinetics, and histamine H1 antagonists.